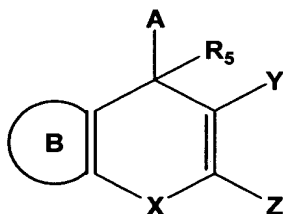


In the Claims:

Please cancel claims 2-4, 8, 10-12, 15, 17, 19-20, 22-24, 29, 31, 43, 48-49, 55-56, 58, 61-62 and 73-74 without prejudice or disclaimer.

Please substitute the following claims 1, 5, 6, 9, 18, 21, 26, 41, 42, 46, 47, 54, 57, 63, 65, 75 and 78 for pending claims 1, 5, 6, 9, 18, 21, 26, 41, 42, 46, 47, 54, 57, 63, 65, 75 and 78:

1. (once amended) A method of treating a disorder responsive to the induction of apoptosis in an animal suffering therefrom, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula I:



or a pharmaceutically acceptable salt or prodrug thereof, wherein:

X is O;

Y is CN;

Z is NR_8R_9 , wherein R_8 and R_9 are independently H or C_{1-4} alkyl;

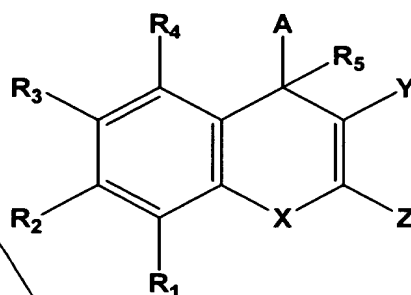
R_5 is hydrogen or C_{1-10} alkyl;

A is optionally substituted C_{6-14} aryl; and

B3
Amended
Sub
C1
cont.
B is an optionally substituted indolo ring.

B4
5. (once amended) The method of claim 1, wherein A is optionally substituted phenyl.

Sub
C2
6. (once amended) The method of claim 1, wherein said compound has the Formula II:



(II)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

(a) R₁-R₄ are independently hydrogen, halo, haloalkyl, aryl, fused aryl carbocyclic, a heterocyclic group, a heteroaryl group, C₁₋₁₀ alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthiol; and R₁ and R₂, or R₂ and R₃, or R₃ and R₄, taken together with the atoms to which they are attached form a pyrrolo group, wherein said group is optionally substituted;

(b) the aryl portion of said arylalkyl, the aryl portion of said arylalkenyl and the aryl portion of said arylalkynyl are each independently C₆₋₁₄ aryl;

- Sub
C2
cont.
- B4
amf
- (c) said carbocyclic is C₃₋₈ cycloalkyl or C₃₋₈ cycloalkenyl;
- (d) said heteroaryl, the heteroaryl portion of said heteroarylalkyl, the heteroaryl portion of said heteroarylkenyl and the heteroaryl portion of said heteroarylalkynyl are each independently selected from the group consisting of thienyl, benzo[b]thienyl, naphtho[2,3-b]thienyl, thianthrenyl, furyl, pyranal, isobenzofuranyl, chromenyl, xanthenyl, phenoxanthiyl, 2*H*-pyrrolyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolizynl, isoindolyl, 3*H*-indolyl, indolyl, indazolyl, purinyl, 4*H*-quinolizynl, isoquinolyl, quinolyl, phthalzyl, naphthyridinyl, quinozalynl, cinnolynl, pteridinyl, carbazolyl, β-carbolynl, phenanthridinyl, acridinyl, perimidinyl, phenanthrolinyl, phenazinyl, isothiazolyl, phenothiazinyl, isoxazolyl, furazanyl, phenoxazinyl, 1,4-dihydroquinoxaline-2,3-dione, 7-aminoisocoumarin, pyrido[1,2-a]pyrimidin-4-one, 1,2-benzisoxazol-3-yl, benzimidazolyl, 2-oxindolyl, 2-oxobenzimidazolyl and the N-oxides thereof; and
- (e) said heterocyclic and the heterocyclic portion of said heterocycloalkyl are each independently selected from the group consisting of tetrahydrofuranyl, pyranal, piperidinyl, piperazinyl, pyrrolidinyl, imidazolidinyl, imidazolynl, indolynl, isoindolynl, quinuclidynl, morpholynl, isochromanyl, chromanyl, pyrazolidinyl, pyrazolynl, tetronoyl and tetramoyl.
-

B5

9. The method of claim 6, wherein R₁ and R₂, or R₂ and R₃, or R₃ and R₄, are taken together to form a structure selected from the group consisting of -CH₂N(R)CH₂-, -N(R)-CH=CH- and -CH=CH-N(R)-, wherein R is hydrogen, C₁₋₁₀ alkyl, haloalkyl,

B5
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aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

B6

18. (once amended) The method of claim 16, wherein R₁ and R₂, or R₂ and R₃, or R₃ and R₄, are taken together to form a structure selected from the group consisting of -CH₂N(R)CH₂-, -N(R)-CH=CH- and -CH=CH-N(R)-, wherein R is hydrogen, C₁₋₁₀ alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

B7

21. (once amended) The method of claim 16, wherein R₁ and R₂ together form an optionally substituted ring, wherein said ring is pyrrolo.

B8

26. (once amended) The method of claim 1, wherein said compound is selected from the group consisting of:

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-8-methyl-4*H*-indolo[4,5-*b*]pyran;

B8
Chief

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

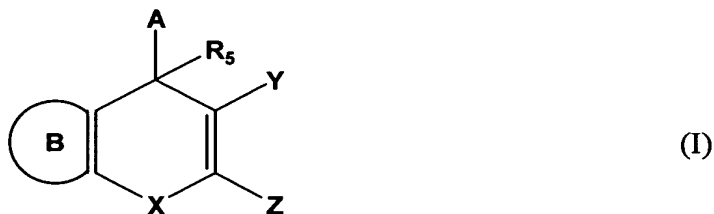
2-Amino-3-cyano-4-(3-nitrophenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3-cyanophenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3,5-dimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran; and

9-Acetamide-2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-
indolo[4,5-*b*]pyran.

41. (once amended) A pharmaceutical composition comprising a
pharmaceutically acceptable excipient or carrier and a compound of Formula I:



or a pharmaceutically acceptable salt or prodrug thereof, wherein:

X is O;

Y is CN;

Z is NR_8R_9 , wherein R_8 and R_9 are independently H or C_{1-4} alkyl;

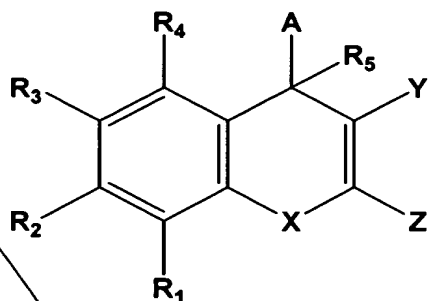
R_5 is hydrogen or C_{1-10} alkyl;

A is optionally substituted C_{6-14} aryl; and

B is an optionally substituted indolo ring.

42. (once amended) The pharmaceutical composition of claim 41, wherein A is optionally substituted phenyl.

46. (once amended) The pharmaceutical composition of claim 41, comprising a pharmaceutically acceptable excipient or carrier and a compound of Formula II:



(II)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

- (a) R₁-R₄ are independently hydrogen, halo, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, C₁₋₁₀ alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthiol; and R₁ and R₂, or R₂ and R₃, or R₃ and R₄, taken together with the atoms to which they are attached form a pyrrolo group, wherein said group is optionally substituted;
- (b) the aryl portion of said arylalkyl, the aryl portion of said arylalkenyl and the aryl portion of said arylalkynyl are each independently C₆₋₁₄ aryl;
- (c) said carbocyclic is C₃₋₈ cycloalkyl or C₃₋₈ cycloalkenyl;

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C5
cont.

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(d) said heteroaryl, the heteroaryl portion of said heteroarylalkyl, the heteroaryl portion of said heteroarylkenyl and the heteroaryl portion of said heteroarylalkynyl are each independently selected from the group consisting of thienyl, benzo[b]thienyl, naphtho[2,3-b]thienyl, thianthrenyl, furyl, pyranal, isobenzofuranyl, chromenyl, xanthenyl, phenoxanthiynyl, 2*H*-pyrrolyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolizynyl, isoindolyl, 3*H*-indolyl, indolyl, indazolyl, purinyl, 4*H*-quinolizynyl, isoquinolyl, quinolyl, phthalzinyll, naphthyridinyl, quinozalinyll, cinnolinyll, pteridinyl, carbazolyl, β -carbolinyll, phenanthridinyl, acrindinyll, perimidinyll, phenanthrolinyll, phenazinyl, isothiazolyl, phenothiazinyll, isoxazolyl, furazanyl, phenoxazinyl, 1,4-dihydroquinoxaline-2,3-dione, 7-aminoisocoumarin, pyrido[1,2-a]pyrimidin-4-one, 1,2-benzoisoxazol-3-yl, benzimidazolyl, 2-oxindolyl, 2-oxobenzimidazolyl and the N-oxides thereof; and

(e) said heterocyclic and the heterocyclic portion of said heterocycloalkyl are each independently selected from the group consisting of tetrahydrofuranyl, pyranal, piperidinyl, piperazinyl, pyrrolidinyl, imidazolidinyl, imidazolinyll, indolinyll, isoindolinyll, quinuclidinyll, morpholinyll, isochromanyll, chromanyll, pyrazolidinyll, pyrazolinyll, tetronoyl and tetramoyl.

47. (once amended) The pharmaceutical composition of claim 46, wherein R₁ and R₂, or R₂ and R₃, or R₃ and R₄, are taken together to form a structure selected from the group consisting of -CH₂N(R)CH₂-, -N(R)-CH=CH- and -CH=CH-N(R)-, wherein R is hydrogen, C₁₋₁₀ alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic

B¹⁰
M¹⁰

group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

B¹¹

54. (once amended) The pharmaceutical composition of claim 53, wherein R₁ and R₂, or R₂ and R₃, or R₃ and R₄, are taken together to form a structure selected from the group consisting of -CH₂N(R)CH₂-, -N(R)-CH=CH- and -CH=CH-N(R)-, wherein R is hydrogen, C₁₋₁₀ alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

B¹²

57. (once amended) The pharmaceutical composition of claim 53, wherein R₁ and R₂ together form an optionally substituted ring, wherein said ring is pyrrolo.

B¹³

63. (once amended) A pharmaceutical composition comprising a pharmaceutically acceptable excipient or carrier and a compound selected from the group consisting of:

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-8-methyl-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-nitrophenyl)-4H-indolo[4,5-b]pyran;

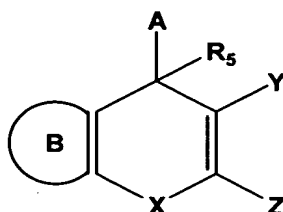
2-Amino-3-cyano-4-(3-cyanophenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran; and

9-Acetamide-2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran.

65. (once amended) The pharmaceutical composition of claim 64, wherein said known cancer chemotherapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosphamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, mitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin®, Rituxan® and alanosine.

75. (once amended) An indolopyran of Formula I:



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

B is optionally substituted indolo;

X is O;

Y is CN;

Z is NR_8R_9 , wherein R_8 and R_9 are independently H or C_{1-4} alkyl;

R_5 is hydrogen or C_{1-10} alkyl; and

A is optionally substituted C_{6-14} aryl.

78. (once amended) A compound selected from the group consisting of:

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-8-methyl-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3-nitrophenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3-cyanophenyl)-4*H*-indolo[4,5-*b*]pyran;

B16
Contd

2-Amino-3-cyano-4-(3,5-dimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran; and
9-Acetamide-2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-
indolo[4,5-*b*]pyran.

Please add the following new claims 79-81:

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B17

~~79. (new) The method of claim 1, wherein said aryl is selected from the group consisting of phenyl, naphthyl, penanthrenyl, anthracenyl, indenyl, azulenyl, biphenyl, biphenylenyl and fluorenyl.~~

80. (new) The pharmaceutical composition of claim 41, wherein said aryl is selected from the group consisting of phenyl, naphthyl, penanthrenyl, anthracenyl, indenyl, azulenyl, biphenyl, biphenylenyl and fluorenyl.

Sub
C7

~~81. (new) The indolopyran of claim 75, wherein said aryl is selected from the group consisting of phenyl, naphthyl, penanthrenyl, anthracenyl, indenyl, azulenyl, biphenyl, biphenylenyl and fluorenyl.~~
